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| 10/534,130 | 12/30/2005 | Ian Hector Frazer | 23558-008US | 8451 |

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| EXAMINER | |
|---|---|
| EPPS -SMITH, JANET L | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/534,130 | FRAZER, IAN HECTOR | |
| | Examiner | Art Unit | |
| | Janet L. Epps-Smith | 1633 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *06 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *39-44,46-58,66-70 and 72-78* is/are pending in the application.

4a) Of the above claim(s) *66-70 and 72-76* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-44,46-58,77 and 78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Response to Amendment/Arguments*

1. Claims 39-44, 46-58, and 77-78 are pending for examination.

2. Claims 66-67, 70, and 74-76 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

### *Claim Rejections - 35 USC § 112*

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 39--44, 46-58, and 77-78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claim 39 recites a method wherein a synthetic polynucleotide is constructed such that it confers an immune response to a target antigen in a mammal of interest in a "different quality" than that conferred by a parent polynucleotide. However, the method further states that the synonymous codon selected to be inserted into the synthetic polynucleotide, is selected on the basis that it exhibits a "different preference of conferring an immune response" than the first codon of the parent polynucleotide. Applicant's arguments and amendments have not addressed the instant rejection to the extent that the terms "different quality" in claim 39, and "different preference" as recited in claim 39 as amended are relative terms which render the claim indefinite, since the relationship between an immune response of a "different quality," and selecting synonymous codon on the basis that it has a "different preference" for an immune

response, is unclear. In regards to the "different quality" limitation, it appears that applicants are referring to the same immune response, wherein the "quality" of the immune response is different with respect to the synthetic polynucleotide in comparison to the parent polynucleotide. In regards to the "different preference," is appears that Applicants are referring to different immune responses entirely.

6. Moreover, Applicants have not provided any means for the skilled artisan to ascertain what the term "quality" is intended to encompass as it relates to an "immune response." The term "quality" in claim 39 is a relative term which renders the claim indefinite. The term "quality" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

7. Claims 40-44, 46-58, and 77-78, which depend from claim 39 are also rejected for the reasons set forth above.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 39-44, 46-58, and 77-78 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (Written Description).

10. Applicant's arguments filed 11-06-08 have been fully considered but they are not persuasive. Applicants traversed the instant rejection on the grounds that the instant claims have been amended to recite "an immune response to a target antigen." According to Applicants one skilled in the art readily would understand that the inventor had full possession of the claimed methods that permit preparation of polynucleotides that can be used to modulate an immune response to a target antigen in a mammal.

11. Contrary to Applicant's assertions, the claims as amended recite the construction of a synthetic polynucleotide which differs from a parent polynucleotide by synonymous codon usage wherein the immune response to a specific target antigen of the synthetic polynucleotide has a "different quality" than that produced by a parent polynucleotide.

12. As stated above, the metes and bounds of the phrase "different quality," are indefinite, it is unclear what the scope of this phrase is intended to encompass.

13. Also, it is clear from the specification as filed that with respect to each parent polynucleotide, a variety of potential synthetic polynucleotide constructs comprising variations in codon usage must first be isolated. The synthetic polynucleotides are then tested for their ability to produce a protective immune response to a target antigen in comparison to the parent polynucleotide. Without further *de novo* experimentation, the ordinary skilled artisan would not be able to predict which synonymous codons to replace in a parent polynucleotide in order to confer an immune response of a "different quality" to a target antigen.

14. To the extent that there is no direct correlation between the structure of full scope of synthetic (i.e. codon optimized) polynucleotides encompassed by the instant claims

and the full scope of "immune responses" of "different quality" encompassed by the instant claims, it is clear that *de novo* experimentation would have to be performed in order to identify those particular preferred codons within a given polynucleotide that are necessary to produce the plurality of "qualities" of immune response to a target antigen encompassed by the instant claims. According to the Guidelines for Examination of Patent Applications Under the 35 USC 112 ¶ 1, "Written Description" Requirement, see January 5, 2001 (Vol. 66, No. 4, pages 1099-1111) Federal Register: "[T]o satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that applicant was in possession of the claimed invention."

15. Claims 39-44, 46-58, and 77-78 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable

one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

16. Applicant's arguments filed 11-06-08 have been fully considered but they are not persuasive. Applicants traversed the instant rejection on the grounds that in light of the amendment to the claims to recite wherein the phenotype is an immune response to an antigen and in response to the Declaration under 37 CFR 1.132 by Dr. Frazer that the full scope of the claimed invention is enabled. Contrary to Applicant's assertions, the guidance provide by Applicants with respect to the design of a synthetic polynucleotide to produce an improved immune response in a mammal against an HPV E7 protein, was not present in the specification as filed, and it is unclear if Applicants followed the teachings in the specification as filed to identify these optimized constructs. As per MPEP § 2164.05:

"[T]o overcome a prima facie case of lack of enablement, applicant must demonstrate by argument and/or evidence that the disclosure, as filed, would have enabled the claimed invention for one skilled in the art at the time of filing. This does not preclude applicant from providing a declaration after the filing date which demonstrates that the claimed invention works. However, the examiner should carefully compare the steps, materials, and conditions used in the experiments of the declaration with those disclosed in the application to make sure that they are commensurate in scope; i.e., that the experiments used the guidance in the specification as filed and what was well known to one of skill in the art. Such a showing also must be commensurate with the scope of the claimed invention, i.e., must bear a reasonable correlation to the scope of the claimed invention."

17. The Declaration under 37 CFR 1.132 filed 11-06-2008 is insufficient to overcome the rejection of claims 39-44, 46-58, and 77-78 based upon 35 USC 112, 1st paragraph as set forth in the last Office action because: Applicant's Declaration provided guidance regarding the ranking of immune response preferences for synonymous codons.

However, this guidance was not present in the specification as originally filed. Moreover, it is unclear that the ranking of immune response was identified was based upon the teachings of the specification, or if Applicants utilized some other method for identifying these codons. Moreover, it is unclear if the optimized codons are consistent with respect to an immune response against any antigen, or if the information provided is limited to only the production of the E7 protein.

18. As stated in the prior Office Action, Applicant's disclosure of Examples 1-4 does not provide the skilled artisan with sufficient guidance for practicing the full scope of the claimed invention without need for undue experimentation.

***Claim Rejections - 35 USC § 102 & 103***

19. The rejections under 35 USC 102 and 103 are withdrawn in response to Applicant's amendment filed 11-06-08.

***Conclusion***

20. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Smith whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Epps-Smith/
Primary Examiner, Art Unit 1633